CLAIMS

1. A method for determining circulating microparticles and/or stimulated procoagulant cells comprising:

   (a) mixing a sample containing said circulating microparticles and/or stimulated procoagulant cells with a specific receptor for a compound exposed on said microparticles and procoagulant cells which receptor is bound directly or indirectly to a solid phase under conditions to form a complex of the solid phase bound receptor and the microparticle and/or procoagulant cell,

   (b) separating the solid phase from the liquid phase,

   (c) determining the amount of microparticles and/or procoagulant cells on the solid phase or after separation of the solid phase by appropriate methods.

2. The method of claim 1, wherein the specific receptor in step (a) is annexin V.

3. The method of claim 2, wherein in step (a) calcium ions are added.

4. The method of claims 1 to 3, wherein the specific receptor is bound to the solid phase via a specific binding pair comprising a first and a second binding pair member (bpm), the first bpm is attached to the solid phase and the second bpm is coupled to the specific receptor.

5. The method of claim 1, wherein in step (c) the amount of microparticles and/or procoagulant cells is determined by detecting the activation of prothrombin (factor II) to thrombin (factor IIa).

6. The method of claim 5, wherein in step (a) inhibitors of thrombin and/or Factor Xa are present.

7. The method of claims 5 and 6, wherein the activation of prothrombin to thrombin is detected by mixing the microparticles and/or procoagulant cells with a reagent comprising factor V, factor Xa, prothrombin (factor II) and calcium-ions for an appropriate time interval, stopping the reaction by complexation of the calcium-ions, and determining thrombin by its ability to hydrolyse a chromogenic substrate.

8. A method for determining circulating microparticles and/or stimulated procoagulant cells comprising:

(a) mixing a sample containing said circulating microparticles and/or stimulated procoagulant cells with a specific receptor for a compound exposed on said circulating microparticles and/or stimulated procoagulant cells under conditions to form a complex of the circulating microparticles and/or stimulated procoagulant cells and the receptor,

(b) determining the amount of microparticles and/or stimulated procoagulant cells.

9. The method of claim 8, wherein the receptor is at least bivalent and the determination in step (b) is done by nephelometric or turbidimetric measurement.

10. The method of claims 8 and 9, wherein the specific receptor is a receptor-coated particle.

11. The method of claim 10, wherein the specific receptor is an annexin-V-coated particle.

12. The method of claim 10, wherein the receptor-coated particle is an avidin or strept-avidin-coated particle to which a biotinylated receptor is bound.

13. A method for determining a special category or subgroup of circulating microparticles and/or stimulated procoagulant cells comprising:

(a) mixing a sample containing said circulating microparticles and/or stimulated procoagulant cells with a specific receptor 1 for a compound exposed on said microparticles and stimulated procoagulant cells which receptor is bound directly or indirectly to a solid phase under conditions to form a complex of solid phase bound receptor 1 and microparticle or stimulated procoagulant cell,

(b) optionally separating the solid phase from the liquid phase,

(c) binding of a receptor 2 to the microparticles and/or procoagulant cells which receptor 2 is specific for a marker of the special category or subgroup of microparticles and stimulated procoagulant cells,

(d) determining the complex of receptor 1, microparticles or stimulated procoagulant cells and receptor 2 by appropriate methods.

14. The method of claim 13, wherein steps (a) and (c) are conducted simultaneously.

15. The method of claims 13 and 14, wherein the receptor 2 is an antibody to a marker of thrombocytes such as GPIb, GPIX, GPIIb/IIIa, thrombospondin or a marker for endothelial cells such as thrombomodulin or a marker for monocytes such as CD14.

16. A method for determining a special category or subgroup of circulating microparticles and/or stimulated procoagulant cells comprising:

(a) mixing a sample containing said circulating microparticles and/or stimulated procoagulant cells with a receptor for the subgroup-specific compound exposed on said circulating microparticles and/or stimulated procoagulant cells,

(b) determining the binding of circulating microparticles and/or stimulated procoagulant cells to said receptor by appropriate methods.

17. The method of claim 16, wherein the receptor for the subgroup-specific compound is bound directly or indirectly to a solid phase.

18. The method of claim 17, wherein the solid phase is a particle such as a latex particle and the determination of the binding of the circulating microparticles and/or stimulated procoagulant cells to said receptor is accomplished by measurement of the agglutination of the particles.

19. The method of claim 17, wherein after step (a) the solid phase is separated from the liquid phase.

20. The method of claim 19, wherein in step (b) the binding is determined by detecting the activation of prothrombin (factor II) to thrombin (factor IIa).

21. A method for determining phospholipid-binding antibodies in a sample comprising:

(a) mixing the blood sample with microparticles and/or procoagulant cells or synthetic phospholipid-containing liposomes under conditions to allow the binding of phospholipid-binding antibodies present in said blood sample to said microparticles or stimulated procoagulant cells or synthetic phospholipid-containing liposomes,

(b) determining the binding of phospholipid-binding antibodies by appropriate methods.

22. The method of claim 21, wherein in step (b) the antibodies are determined by measurement of the precipitation of the circulating microparticles and/or stimulated procoagulant cells or synthetic phospholipid-containing liposomes.

23. The method of claim 21, wherein the circulating microparticles and/or stimulated procoagulant cells or synthetic phospholipid-containing liposomes are bound to a solid phase.

24. ~~The method of claim 23, wherein biotinylated circulating microparticles and/or~~ stimulated procoagulant cells or synthetic phospholipid-containing liposomes are bound to a streptavidin- or avidin-coated solid phase.

25. The method of claim 24, wherein the circulating microparticles and/or stimulated procoagulant cells and synthetic phospholipid-containing liposomes are biotinylated by adding biotinylated phosphatidylethanolamine or biotinylated phosphatidylcholine.

26. The method of claim 24, wherein the synthetic phospholipid-containing liposomes are biotinylated by producing said liposomes in the presence of biotinylated phosphatidyl-ethanolamine and/or biotinylated phosphatidyl-choline.

27. The method of claim 23 wherein the circulating microparticles and/or stimulated procoagulant cells or synthetic phospholipid-containing liposomes are bound to an annexin-V-coated solid phase.

28. The method of claims 21 to 27, wherein said circulating microparticles and/or stimulated procoagulant cells or synthetic phospholipid-containing liposomes further comprising proteins for example ß2-glycoprotein 1, prothrombin, protein S or protein C.

29. A method for the diagnosis of vascular diseases such as peripheral artherial occlusion, artheriosclerosis, diabetic angiopathy, vasculitis, pre-eclampsia, lupus erythematosus or angina pectoris by determining the circulating microparticles and/or stimulated procoagulant cells.

30. A method for determining the prethrombotic state of an individual or for monitoring the state of an individual after PTCA by determining circulating microparticles and/or stimulated procoagulant cells.

31. A method for the diagnosis of diseases associated with cell damage or cell death such as AIDS, cancer or paroxysmal nocturnal hemoglobinuria by determining the ~~circulating apoptotic bodies.~~

~~32. A reagent for determining circulating microparticles and/or stimulated procoagulant~~ cells comprising:

a specific receptor for a compound exposed on said microparticles and procoagulant cells

and further compounds necessary for determining the amount of binding of the specific receptor to said microparticles and procoagulant cells.

33. A reagent for determining a special category or subgroup of circulating microparticles and/or procoagulant cells comprising:

a receptor which is specific for a marker of the special category or subgroup of microparticles and stimulated procoagulant cells,

and further compounds necessary for determining the amount of binding of both receptors to said microparticles and procoagulant cells.

34. A reagent according to claim 32 further comprising a receptor which is specific for a compound exposed on said microparticles and stimulated procoagulant cells.

35. A reagent for determining phospholipid-binding antibodies comprising:

microparticles and/or procoagulant cells or synthetic phospholipid-containing liposomes

and further compounds necessary for determining the binding of phospholipid-binding antibodies on said microparticles, procoagulant cells or synthetic phospholipid-containing liposomes.